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Attorney Docket No. 970232/HG

Transmitted herewith for filing is the patent application of

Inventor(s):

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Title:

COMPOSITION FOR TREATING CONDYLOMA ACUMINATA

Priority Claim (35 U.S.C. 119) is made, based upon:

Japanese Patent Application No. 321195/1996 filed November 18, 1996.

Enclosed herewith are:

- ☒ Specification (Description, Claims, Abstract): Pages 1 - 10 ; Number of claims 1 - 8
- ☒ Declaration and Power of Attorney (executed)
- ☐ TO BE POST-FILED: SIGNED DECLARATION UNDER 37 CFR 1.53(d) UNEXECUTED DECLARATION ENCLOSED FOR INFORMATION PURPOSES ONLY
- ☐ Sheets of drawings, Figures 1 - [ ] Formal [ ] Informal
- ☒ Assignment and Form PTO-1595 Recordation Form Cover Sheet
- ☐ Certified copy (ies) of priority document(s) identified above
- ☐ Information Disclosure Statement including Form PTO-1449
- ☐ Preliminary Amendment
- ☐ Verified Statement(s) Claiming Small Entity Status
- ☒ Receipt Postcard

	Number Filed		Number Extra	Rate	Calculations
Total Claims	8 -20 =		0	x \$22.00 =	\$ --
Independent Claims	2 - 3 =		0	x \$80.00 =	\$ --
MULTIPLE DEPENDENT CLAIMS				+ \$260.00 =	\$ --
ASSIGNMENT RECORDING FEE				BASIC FEE	\$ 770.00
					\$ 40.00
				Total of above Calculations	\$ 810.00

To the extent not tendered by check, authorization is given to charge any fees under 37 CFR 1.16 and 1.17 during pendency of the application, or to credit any overpayment, to Deposit Account No. 06-1378. Duplicate copy of this letter is enclosed.

FRISHAUF, HOLTZ, GOODMAN, LANGER & CHICK, P.C.

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COMPOSITION FOR TREATING CONDYLOMA ACUMINATA

FIELD OF THE INVENTION

The present invention relates to a composition for treating Condyloma acuminata, or more specifically to a composition for treating Condyloma acuminata caused by human papillomavirus, containing tea catechin as a main component.

BACKGROUND OF THE INVENTION

Condyloma acuminata is a wart detectable on the skin or mucous membrane of the genital organs of men and women, and is caused by human papilloma virus (HPV). The site of infection in men is the balanic area, coronary sulcus, foreskin, anal area, urethral meatus; and in women is the vagina, labium, anal area and urethral orifice. Clinical symptoms appear from 1-6 months, on average 3 months after infection, but usually symptoms are not noticed by the patient. This wart shows distinctive papillary or cockscomb-like tumors and has a tendency to accumulate and multiply and is usually red or reddish brown in colour. Detection of HPV in condyloma acuminata is by a method of taking tissue or a smear from the infected area and determining the DNA of the virus.

According to this method the detection rate is almost 100%. Types HPV6 and 11 of the virus are the ones most commonly detected and because HPV16 has been detected in malignant squamous cell carcinoma from cancer of the penis, cancer of the cervix and Condyloma acuminata, there is a strong possibility that HPV16 is related to the malignancy of Condyloma acuminata.

Means for a treatment of Condyloma acuminata caused by human papilloma virus which have been tried at present are by physical means such as surgical excision, electrocauterization, cryosurgery, laser therapy etc. and medication such as applications of Podophyllin, 5-Fluorouracil, Bleomycin, Interferon etc. are presently available. However surgical treatment is distressing for the patient, considering the site of infection, and with topical applications there is the concern of side-effects. Because of this no conclusive treatment is presently available.

Condyloma acuminata has a high rate of recurrence, and a complete cure is difficult unless treated constantly. Because of this a treatment which has a high degree of safety and is convenient is strongly desired.

#### SUMMARY OF THE INVENTION

Thus for the treatment of condyloma acuminata caused by human papillomavirus, desired is a treatment which is easy for the patient to take, for example a medication which can be applied to the affected area by the patient themselves showing good results in a relatively short period of use and having no side-effects.

#### DESCRIPTION OF THE INVENTION

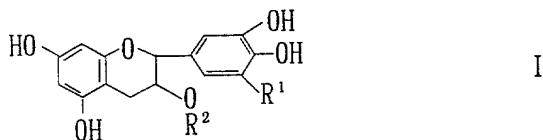
We, the present inventors looked for a natural substance which has no side-effects, may be safely applied for a long period of time by the patient themselves and is notably effective; and after extensive testing we discovered that catechin, a component of tea which is an everyday beverage, is effective and thus the present invention was

developed.

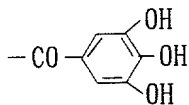
Thus the present invention relates to a composition for a treatment of Condyloma acuminata caused by human papillomavirus containing tea catechin as a main component.

#### DETAILED DESCRIPTION OF THE INVENTION

The tea catechin of the present invention is shown below in the general formula 1



wherein R<sup>1</sup> represents H or OH and R<sup>2</sup> represents H or



The tea catechins are more specifically, epicatechin, epicatechin gallate, epigallocatechin gallate, gallocatechin etc. (including derivatives thereof). These catechins can be used singly or two or more may be mixed together. Out of these it is particularly desirable to have (-)-epigallocatechin gallate as a main component. For example: Polyphenon 100<sup>TM</sup> (produced by Mitsui Norin Co.; Composition: (+)-gallocatechin 1.44%, (-)-epicatechin 5.81%, (-)-epigallocatechin 17.57%, (-)-epicatechin gallate 12.51%, (-)-epigallocatechin gallate 53.90%); or Polyphenon E<sup>TM</sup> (produced by Mitsui Norin Co.; Composition: (-)-epicatechin 10.8%, (-)-epigallocatechin 9.2%, (-)-epicatechin gallate 6.5%, (-)-epigallocatechin gallate 54.8%, (-)-gallocatechin

gallate 4.0%).

The treatment for Condyloma acuminata of the present invention could be used for example in the form of ointment such as a cream, jelly, emulsion; or in the form of suppository such as a capsule, and usually the tea catechin component is combined with an excipient, extending agent, emulsifier, dispersing agent etc. Vaseline is suitable as a base for the ointment. For the ointment the content of tea catechin should be between 5-20% by weight, preferably between 12-18% by weight, more preferably 15% by weight. In the case of suppository the content of tea catechin should be 100-500mg/capsule, preferably 200-300mg/capsule, or more preferably 250mg/capsule.

A typical usage example for the ointment is to apply directly to the infected area of the external genital organs or vagina, a vaseline cream containing 5-20% by weight catechin, from once to several times everyday for a period of 1-2 months. A typical usage example for the suppository in the case where for example the infected area is the cervix or the vagina is to insert a capsule containing 100-500mg tea catechin, from once to several times everyday for a period of 1-2 months.

There is no danger of side-effects from the treatment for condyloma acuminata with the composition of the present invention having tea catechin as the main component thereof since the main component is a natural substance derived from tea which is commonly consumed regularly, and it may be taken for long periods of time. Moreover this medication may be easily applied to or inserted in the infected area by the patient themselves. The composition of the present invention for a treatment of condyloma acuminata has a very high potential for practical use.

Another aspect of the invention is a method of applying an effective treating human papilloma virus-infected Condyloma acuminata amount of tea catechin to an infected area of a patient to treat human papilloma virus-infected Condyloma acuminata.

#### Examples

The present invention will be explained in more detail with reference to the following examples which are in no way meant to limit the scope of the invention.

#### Test Example 1

An ointment consisting essentially of a vaseline based vaginal lubricant containing, as the main component, tea catechin (Trade name: Polyphenon 100, produced by Mitsui Norin Co. Ltd., its main component: (-)-epigallocatechin gallate) was applied to the cervix of healthy mice (50 mice in a group) in catechin dosages of 8mg, 15mg, or 38mg for a period of 7 consecutive days. After this time pathological and histological examinations were carried out and it was determined that except for a mild inflammatory reaction in the cervix of the mice of the 38mg dose group no toxic effect was observed.

#### Example 1

Clinical tests of the present invention were carried out at the Cancer Institute, Chinese Academy of Medical Sciences in Beijing with a group of 15 women who had been diagnosed with HPV-infected condyloma acuminata. All patients were confirmed to have condyloma in the vulva (external genital organs), vagina and/or cervix according to clinical examination, cytologic, colposcopic and pathologic tests. Two of the fifteen patients were confirmed to be infected in two areas. Warts were from 0.2 to 2cm in diameter.

Tests were carried out on these 15 patients using an ointment containing 10-15% of vaseline based vaginal lubricant and 5-20% of tea catechin (Trade name: Polyphenon 100, produced by Mitsui Norin Co. Ltd., crude catechin content is about 90% and its main component is (-)-epigallocatechin gallate) or using a suppository containing 100-500mg/capsule of the above tea catechin. Applying the ointment to the external genital organs and applying the suppository to the vagina and cervix, the treatments of the present invention were used continuously once a day for about two months.

During the period of treatment examinations and colposcopic tests of the infected areas were carried out. Results obtained are shown in Table 1. As shown in the table, when the infected area completely disappeared it was judged to be cured, when 50% or more disappeared it was judged to be improved and when less than 50% or nothing disappeared it was judged there was no effect.

Table 1

Infected Area	No. of Patients	Cured	Improved	No Effect
External genital organs	9	4	3	2
Vagina	6	9	1	5
Cervix	2	1	0	1
Total (%)	17	5 (29.4)	4 (23.5)	8 (47.1)

As is evident from the table, 7 cases out of 9 (77.8%) of condyloma acuminata of the external genital organ showed a clear effect (being either cured or improved). In one case of the cervical infection

the tumor completely disappeared, thus cured. During this period, apart from some patients who experienced slight pain or inflammation in the infected area and a few other patients who felt some itching, there were no obvious side-effects observed.

#### Example 2

The clinical tests at the Cancer Institute, Chinese Academy of Medical Sciences in Beijing were conducted in the same manner as in Example 1 with a group of 33 female patients diagnosed with HPV-infected condyloma acuminata. In this group, 8 of the patients were infected in two areas. Results are shown in Table 2. As is evident from the table, 92% of condyloma acuminata of the external genital organs and 70% of the vaginal condyloma acuminata was cured or improved, and in the case of the cervical condyloma acuminata, all cases were cured. 25 cases out of 41 cases showed the result as cured and the curing ratio was 61%.

Table 2

Infected Area	No. of Patients	Cured	Improved	No Effect
External genital organs	26	18	6	2
Vagina	10	2	5	3
Cervix	5	5	0	0
Total (%)	41	25 (61.0)	11 (26.8)	5 (12.2)

#### Example 3

The clinical test at the Cancer Institute, Chinese Academy of Medical Sciences in Beijing was conducted in the same manner as in



Example 1 with a group of 22 female patients diagnosed with HPV-infected condyloma acuminata. Results are shown in Table 3. As is evident from the table, out of 16 cases of condyloma acuminata of the external genital organs 7 were cured and 6 improved; a total of 13 (81.3%) being effected. In the case of condyloma acuminata of the vagina, out of 6 cases 3 were cured and 2 were improved; a total of 83.3% was confirmed to be effected.

Table 3

Infected Area	No. of Patients	Cured	Improved	No Effect
External genital organs	16	7	6	3
Vagina	6	3	2	1
Total (%)	22	10 (45.5)	8 (36.4)	4 (18.2)

The entire disclosure of Japanese Patent Application No. 8-321195 filed on November 18, 1996 including specification, claims and summary are incorporated herein by reference in its entirety.

WHAT IS CLAIMED IS:

1. A composition for a treatment of HPV-infected Condyloma acuminata which comprises containing tea catechin as a main component.
2. The composition according to claim 1, wherein tea catechin has (-)-epigallocatechin gallate as the main component.
3. The composition according to claim 1, wherein said composition is in the form of an ointment having 5-20% by weight of tea catechin.
4. The composition according to claim 1, wherein said composition is in the form of a suppository having 100-500mg/capsule.
5. A method of curing Condyloma acuminata caused by human papillomavirus, comprising treating an infected area with a composition which comprises containing tea catechin as a main component.
6. The method according to claim 5, wherein the composition is in the form of an ointment or a suppository.
7. The method according to claim 5, wherein said composition is in the form of an ointment having 5-20% by weight of tea catechin.
8. The method according to claim 5, wherein said composition is in the form of a suppository having 100-500mg/capsule.

ABSTRACT OF THE DISCLOSURE

A composition for a treatment of HPV-infected Condyloma acuminata which comprises containing tea catechin as a main component. This medication has no danger of side-effects and may be easily applied to or inserted in the infected area by the patient themselves.

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**APPLICATION FOR UNITED STATES LETTERS PATENT****Declaration and Power of Attorney**

As a below named inventor, I declare that:

My residence, post office address and citizenship are as stated below next to my name; I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**COMPOSITION FOR TREATING CONDYLOMA ACUMINATA**

the specification of which is attached hereto.

I have reviewed and understand the contents of said specification, including the claims.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56.


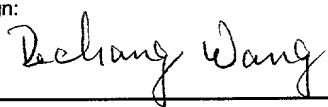

I claim priority benefits under 35 USC §119 of: (i) any foreign application(s) for patent or inventor's certificate listed below; or (ii) any United States provisional application(s) listed below; and have also identified below any foreign application(s) for patent or inventor's certificate, or PCT international application having a filing date before that of the application(s) on which priority is claimed.

COUNTRY	APPLICATION NUMBER	DATE (day, month, year)	PRIORITY CLAIMED
Japan	321195/1996	18.11.1996	yes <u>X</u> no _____
			yes _____ no _____

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I appoint the following attorneys to prosecute this application and to transact all business in the U.S. Patent & Trademark Office connected therewith: Stephen H. Frishauf, Reg. No. 16,233; Leonard Holtz, Reg. No. 22,974; Herbert Goodman, Reg. No. 17,081; Thomas Langer, Reg. No. 27,264; Marshall J. Chick, Reg. No. 26,853; Walter J. Baum, Reg. No. 20,641; Richard S. Barth, Reg. No. 28,180; Douglas Holtz, Reg. No. 33,902; and Robert P. Michal, Reg. No. 35,614.

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